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The Relationship of HDL-Apolipoprotein A-I and HDL-Cholesterol to Risk Factors of Coronary Heart Disease: Initial Results of the Prospective Epidemiological Study in Company Employees in Westfalia

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Summary: In a prospective epidemiologic study in company employees in Westfalia aimed at improving early diagnosis of coronary heart disease in 3069 men and 1387 women, concentrations of HDL-apolipoprotein A-I and HDL-cholesterol were measured and the results were correlated with several risk factors of coronary heart disease. A negative correlation between hypertriglyceridaemia and HDL-cholesterol ($r = -0.25\,♂; -0.27\,♀; p < 0.001$) and between relative body weight and HDL-cholesterol ($r = -0.21\,♂; -0.20\,♀; p < 0.001$) could be shown but not between hypertriglyceridaemia and HDL-apolipoprotein A-I and between relative body weight and HDL-apolipoprotein A-I. In cigarette smokers HDL-apolipoprotein A-I as well as HDL-cholesterol were found to be lower than in non-smokers. On the other hand HDL-apolipoprotein A-I but not HDL-cholesterol was positively correlated with systolic and diastolic blood pressure.

Die Beziehung von HDL-Apolipoprotein A-I und HDL-Cholesterin zu Risikofaktoren der koronaren Herzkrankheit: Erste Ergebnisse der prospektiven epidemiologischen Studie bei Betriebsangehörigen im Raum Westfalen

Zusammenfassung: In einer prospektiven epidemiologischen Studie bei Betriebsangehörigen im Raum Westfalen zur Verbesserung der Frühdiagnostik der koronaren Herzkrankheit wurden die Konzentrationen von HDL-Apolipoprotein A-I und HDL-Cholesterin bei 3069 Männern und 1387 Frauen untersucht und die Ergebnisse mit den verschiedenen Risikofaktoren der koronaren Herzkrankheit korreliert. Nur für HDL-Cholesterin, aber nicht für HDL-Apolipoprotein A-I wurde eine negative Korrelation zur Triglyceridkonzentration ($r = -0{,}25\,♂; -0{,}27\,♀; p < 0{,}001$) und zum relativen Körpergewicht ($r = -0{,}21\,♂; -0{,}20\,♀; p < 0{,}001$) beobachtet. Bei Zigarettenrauchern waren sowohl die Konzentrationen von HDL-Apolipoprotein A-I als auch von HDL-Cholesterin niedriger als bei Nichtrauchern. Auf der anderen Seite war HDL-Apolipoprotein A-I, nicht jedoch HDL-Cholesterin, positiv mit dem systolischen und diastolischen Blutdruck korreliert.

Introduction

In epidemiological (1–5) and clinical studies (6–7) the determination of HDL-cholesterol in addition to the analysis of total cholesterol and triglycerides has been shown to improve the detection of the risk of coronary heart disease. The possible relationship of other HDL constituents (e.g. apolipoproteins A-I and A-II, phosphatidylcholine, sphingomyelin) to the risk of coronary heart disease is not yet known. Though several clinical studies have indicated decreased levels of apolipoprotein A-I in subjects with coronary heart disease (7, 8, 11), there is still a lack of prospective epidemiological data to demonstrate the predictive power of HDL-apolipoproteins with respect to coronary heart disease.

The present paper reports initial results of our epidemiological studies (12) with regard to the correlation of HDL-apolipoprotein A-I with several risk factors of coronary heart disease.

Subjects and Methods

3069 male and 1387 female company employees from four different companies in the Westfalia region were studied ("Prospective epidemiologic study in company employees in

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Westfalia"). In a special bus, blood was collected in the morning after a 12 h fast and was allowed to clot for 30 min at room temperature. After removing cells by centrifugation at 3000 min^{-1}, the serum was stored at 4 °C and was transported to our laboratory within 3 days maximum. Experiments were performed within 25 hours after receiving the samples. Serum levels of cholesterol, triglycerides, glucose and uric acid were determined with the SMAC Autoanalyzer (Technicon GmbH., Bad Vilbel, GFR) as described elsewhere (12).

For determination of HDL-cholesterol, apolipoprotein B-containing lipoproteins were precipitated using the phosphotungstate/$MgCl_2$ precipitation method (13). LDL-cholesterol was calculated from total cholesterol, and HDL-cholesterol and triglycerides according to the formula of *Friedewald* (14). HDL-apolipoprotein A-I was measured by rate nephelometry. Details have been described elsewhere (13).

Results

The means and ranges for HDL-apolipoprotein A-I and HDL-cholesterol for males and females in our prospective epidemiological study are shown in table 1. Females exhibited obviously higher levels of HDL-apolipoprotein A-I and HDL-cholesterol than males. In both sexes levels of HDL-apolipoprotein A-I and HDL-cholesterol were normally distributed.

The results of the correlation analysis of HDL-cholesterol, HDL-apolipoprotein A-I, age and several risk factors of coronary heart disease are shown in table 2.

In males and females HDL-apolipoprotein A-I levels were positively correlated with age, while a positive correlation between HDL-cholesterol and age was found in females but not in males. Furthermore, in both sexes there were obviously significant positive correlations between HDL-apolipoprotein A-I and HDL-cholesterol (males r = 0.66, females r = 0.68), HDL-apolipoprotein A-I and serum cholesterol (males r = 0.21, females r = 0.27), HDL-apolipoprotein A-I and uric acid (males r = 0.12, females r = 0.08) and HDL-apolipoprotein A-I and systolic blood pressure (males r = 0.07, females r = 0.11). A negative correlation was calculated between HDL-apolipoprotein A-I and cigarette smoking (males r = – 0.09, females r = – 0.12).

In contrast to HDL-apolipoprotein A-I, HDL-cholesterol was not positively correlated with uric acid or systolic and diastolic blood pressure. In both sexes HDL-cholesterol showed a close negative correlation with triglycerides (males r = – 0.25, females r = – 0.27), body weight (males r = – 0.21, females r = – 0.20) and cigarette smoking (males r = – 0.05, females r = – 0.11). The most prominent result was the lack of a negative correlation between HDL-apolipoprotein A-I and triglycerides or HDL-apolipoprotein A-I and body weight, respectively, in males and females.

Tab. 1. HDL-apolipoprotein A-I and HDL-cholesterol concentration in company employees in Westfalia.

	HDL-apolipoprotein A-I (g/l)		HDL-cholesterol (g/l)	
	men n=3032	women n=1387	men n=3069	women n=1380
Mean	1.363	1.469	0.4384	0.5326
Standard deviation	0.231	0.252	0.1179	0.1382
Median	1.348	1.457	0.4196	0.5185
Minimum	0.61	0.74	0.16	0.21
Maximum	2.44	2.66	1.47	1.15
5% percentile	1.02	1.07	0.27	0.33
25% percentile	1.21	1.30	0.36	0.43
75% percentile	1.50	1.63	0.50	0.61
95% percentile	1.76	1.88	0.65	0.77

Tab. 2. Coefficients of correlation between HDL-cholesterol and risk factors and between HDL-apolipoprotein A-I and risk factors (prospective epidemiological study in company employees in Westfalia).

	Males, n = 3032		Females, n = 1380	
	HDL-cholesterol	HDL-apolipoprotein A-I	HDL-cholesterol	HDL-apolipoprotein A-I
Age	0.03	0.12[3]	0.14[3]	0.18[3]
HDL-cholesterol		0.66[3]		0.68[3]
HDL-apolipoprotein-A-I	0.66[3]		0.68[3]	
LDL-cholesterol	–0.05[2]	0.03	–0.02	0.04
Cholesterol	0.09[3]	0.21[3]	0.23[3]	0.27[3]
Triglycerides	–0.25[3]	0.01	–0.27[3]	0.03
Glucose	–0.05[1]	0.06[2]	–0.08[2]	0.03
Uric acid	–0.02	0.12[3]	–0.09[2]	0.08[2]
Systolic blood pressure	0.03	0.07[3]	0.00	0.11[3]
Diastolic blood pressure	–0.00	0.04[1]	–0.00	0.08[1]
Relative body weight (*Broca*-index)	–0.21[3]	0.00	–0.20[3]	–0.00
Cigarette smoking	–0.05[1]	–0.09[3]	–0.11[3]	–0.12[3]

[1]) $p < 0.05$
[2]) $p < 0.01$
[3]) $p < 0.001$

Discussion

High density lipoproteins comprise a heterogenous mixture of macromolecules which differ with regard to particle size, chemical composition and physicochemical properties. It is impossible to calculate HDL mass from HDL-cholesterol because the content of the cholesterol moiety in HDL is ranged between 10–20% of HDL mass. In hypertriglyceridaemic sera the cholesterol content of HDL particles is lowered while the triglyceride content of these particles is enhanced (15).

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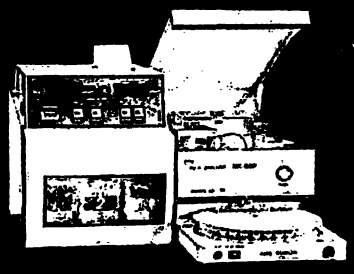

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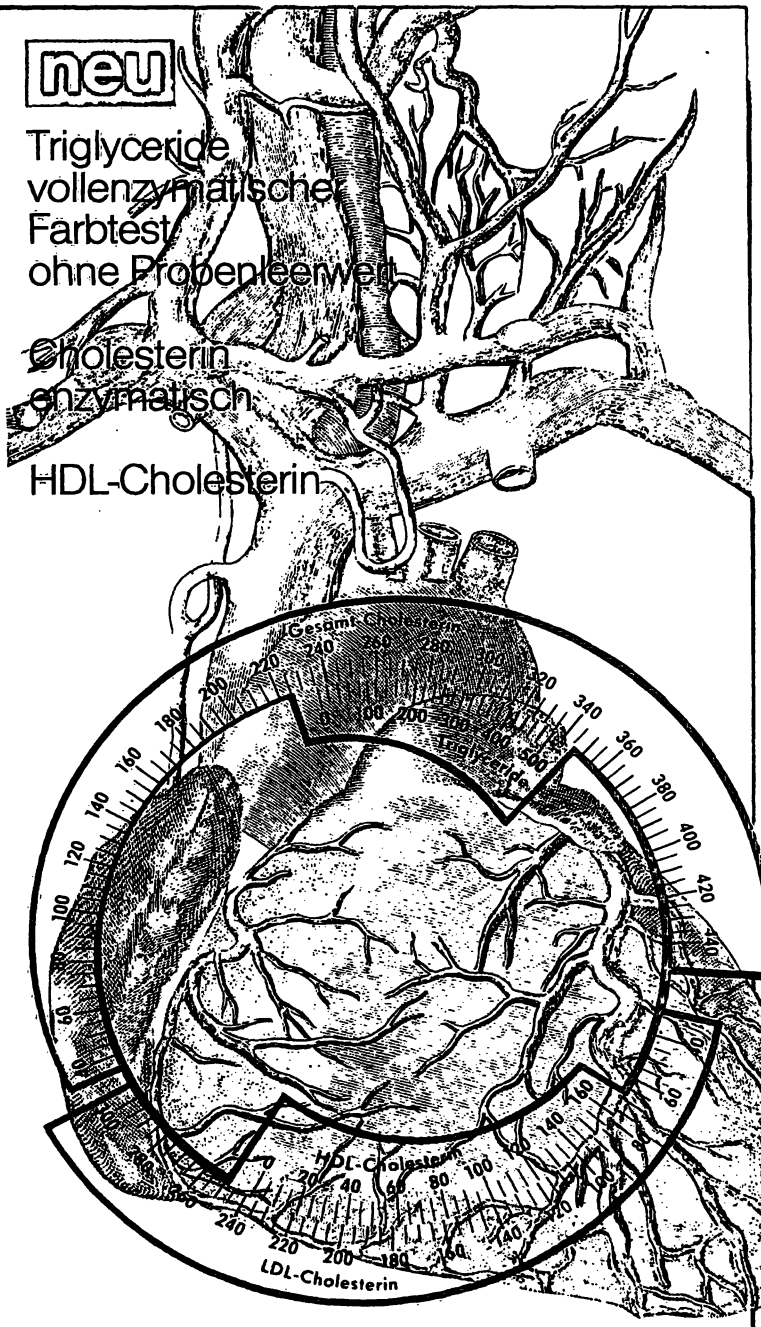

Aussagen über das Risiko arteriosklerotischer Gefäßerkrankungen sind durch die Bestimmung des Gesamtcholesterins und der Triglyceride im Serum möglich; darum sind diese beiden Bestimmungen als Basisprogramm der Lipiddiagnostik anzusehen. Die zusätzliche Bestimmung des HDL-Cholesterins erlaubt weitere fundierte diagnostische Aussagen.

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In light of the heterogeneity of HDL the well-known association between HDL-cholesterol and coronary heart disease does not necessarily reflect a similar association between HDL mass and coronary heart disease or between HDL-apolipoproteins and coronary heart disease. In contrast to HDL-cholesterol the predictive power of other HDL constituents, especially HDL-apolipoproteins, has not been established in prospective studies. According to studies by *Avogaro* et al. on survivors of myocardial infarction (10), or *Bradby* et al. on patients with peripheral vascular disease (8), HDL-apolipoprotein A-I may be a better discriminator between atherosclerotic subjects and controls than HDL-cholesterol.

In other clinical reports, however (9, 11), the superiority of HDL-apolipoprotein A-I as compared to HDL-cholesterol could not be shown. The preliminary results of our prospective epidemiological study show that HDL-cholesterol and HDL-apolipoprotein A-I may exhibit a different relationship to coronary risk.

The negative correlation between HDL-cholesterol and hypertriglyceridaemia and between HDL-cholesterol and obesity could not be demonstrated for HDL-apolipoprotein A-I. In cigarette smokers HDL-cholesterol as well as HDL-apolipoprotein A-I were found to be lower than in non-smokers.

On the other hand HDL-apolipoprotein A-I but not HDL-cholesterol was positively correlated with systolic and diastolic blood pressure. The possible implications of these observations remain to be determined.

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